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EXAMINER	
O'FARRELL, THOMAS JOHN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 12/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,087	YANG ET AL.	
	Examiner	Art Unit	
	Thomas J. O'Farrell	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/29/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1-8 are pending in the instant application. Claim 9 has been cancelled. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following arguments are either necessitated by amendment or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Rejections

Claim Rejections - 35 USC § 112

3. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding instant claim 1.c reciting "passing said hybridized DNA complex in a random coil state from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of flow through said channel", it is unclear whether the hybridized

DNA complex and/or the fluid flowing through the channel is accelerated in this step. Additionally, it is unclear as to what process actually causes the "acceleration of flow" through the narrow channel. It is also unclear as to whether there is a brief or continuous acceleration of flow in the narrow channel. Additionally, it is unclear as to whether the passage of the DNA complex from a reservoir through a narrow channel or the acceleration of flow through the narrow channel causes the hybridized DNA complex to extend into a substantially linear configuration. Clarification is required.

Response to Arguments

4. The response traverses the rejection. The response notes that claim 1, section c, has been amended and asserts that it clearly states that the DNA is in a fluid carrier, and it is the fluid flow that is accelerated to cause stretching of the DNA, as supported on page 8, lines 13-21, of the specification. The response further asserts that the initial acceleration of the fluid as it enters a channel pulls the DNA along the channel, stretching the DNA when it enters the channel. This argument has been thoroughly reviewed but was not found persuasive. The amended claim 1 is clear in that it is the fluid flow, and the DNA within the fluid, that is accelerated in this step. After reviewing the applicant's argument and the specification, it is still not clear as to what process actually causes the "acceleration of fluid flow" through the narrow channel. It is not clear as to whether passing of the fluid carrier from a reservoir in a microfluidic device through a narrow channel causes the acceleration of the fluid flow or whether the hybridized DNA complex along with the fluid carrier being passed from a reservoir in a

microfluidic device through a narrow channel causes the acceleration of the fluid flow. It is still not clear as to whether there is a brief or continuous acceleration of flow in the narrow channel. The applicant's note in the response that the "initial acceleration of the fluid as it enter the channel pulls the DNA..." but this does not, nor does the specification, specifically address whether the acceleration of fluid flow is brief or continuous in the narrow channel. Additionally, amended claim 1 is silent as to whether the passage of the DNA complex from a reservoir through a narrow channel *or* the acceleration of fluid flow through the narrow channel causes the hybridized DNA complex to extend into a substantially linear configuration and therefore the claim is still unclear. For these reasons and the reasons already made of record, the rejection is maintained.

Claim Rejections - 35 USC § 102

5. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Bensimon et al (herein referred to as Bensimon, U.S. Patent 6,054,327, 102(b) date 04/25/2000).

Several aspects of instant claim 1.c have been broadly interpreted by the examiner. Passing the hybridized DNA complex "from a reservoir in a microfluidic device" is interpreted as moving any portion of the hybridized DNA complex initially in a holding area in a device designed to contain small amounts of liquids. Passing the hybridized DNA complex through a "narrow channel to cause an acceleration of flow

through said channel" is interpreted as moving any portion of the hybridized DNA complex through a small passageway, which involves an acceleration of flow through the passageway.

Bensimon teaches a method of analyzing DNA comprising hybridizing the DNA in solution with probes having fluorescent reagents and then detecting the position of the probes after aligning ("causing said hybridized DNA complex to extend into a substantially linear configuration", instant claim 1.c) the DNA (instant claims 1, 5 and 6; see column 16, lines 50-55, and Fig. 6 of Bensimon). Bensimon also teaches that DNA molecules placed in a channel between cover slips can be aligned by the evaporation flow parallel to a moving meniscus in the channel (instant claim 1.c; see column 2, lines 11-12 and column 3, line 22 and Fig. 6 of Bensimon). Regarding this method of aligning DNA described by Bensimon, DNA molecules in a random coil state fixed at a location in a channel between cover slips is interpreted as the embodiment of the hybridized DNA complex initially being in a "reservoir in a microfluidic device" as recited in instant claim 1.c. In addition, as the meniscus initially moves through the channel between the cover slips, there will be an acceleration of fluid flow in the channel and a portion of the DNA complex will pass through the channel as it extends to a linear configuration (see Fig. 6 of Bensimon). This is interpreted as the embodiment of passing the hybridized DNA complex through a "narrow channel to cause an acceleration of flow through said channel, thereby causing said hybridized DNA complex to extend into a substantially linear configuration;" (recited in instant claim 1.c). Bensimon teaches that the probes used to hybridize to DNA can be oligonucleotides, RNA, DNA, and peptide nucleic acids

(instant claims 5 and 6; see column 13, lines 21-23 and 64-65 of Bensimon). Bensimon also teaches that oligonucleotide probes can be labeled with fluorescent labels and microbeads (instant claims 2-4; see column 11, lines 20-41 and column 14, lines 4-7 of Bensimon). With regard to instant claim 1.d reciting "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex,...", the recitation is interpreted as detecting *one or more* optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex, which is taught by Bensimon (see column 16, lines 50-55 of Bensimon).

Response to Arguments

6. The response traverses this rejection. The response asserts that Bensimon et al. does not disclose or suggest movement of the macromolecules or solvent from a reservoir through a channel and there is no reservoir disclosed by Bensimon from which the macromolecule is moving into the channel. This argument has been thoroughly reviewed but was not found persuasive. It is noted that the specification does not provide express definitions of "reservoir" or "narrow channel" and therefore "reservoir" is broadly interpreted as any holding area and "narrow channel" is interpreted as any small passageway and no defined spatial relationship is interpreted between the "reservoir" and "narrow channel". Therefore, the "reservoir" and "narrow channel" could be the same area as they are interpreted to be in the Bensimon stretching apparatus and movement of part of the DNA molecule from the area between the plates of Bensimon

(see Fig. 6 of Bensimon), which is interpreted as the "reservoir" and "narrow channel", through the channel between the plates can be reasonably interpreted as passing the DNA in a fluid carrier from a reservoir in a microfluidic device through a narrow channel.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., movement of the macromolecule from the reservoir *into* the channel) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). However, if the claim recited movement of the DNA complex "from a reservoir in a microfluidic device *into* a narrow channel", the claim would not specify that the reservoir and narrow channel are necessarily distinct compartments with different structural limitations.

The response also asserts that because Bensimon requires attachment of one end of the macromolecule, there can be no movement of the macromolecule from one place to another. Claim 1 recites passing the DNA complex through a narrow channel. Claim 1 does not recite any limitations with regard to how much of the DNA complex is passed through the channel and therefore movement of all but the fixed end of the DNA complex through the area between the plates as taught by Bensimon in Fig. 6 can be reasonably interpreted as passing the DNA complex through a narrow channel. For these reasons and the reasons already made of record, the rejection is maintained.

7. Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Chan et al (hereinafter referred to as Chan-1; Pre Grant Publication 2003/0059822, 102(e) date 09/18/2001).

Chan-1 teaches a method of analyzing a polymer comprising labeling the polymer with first and second unit specific makers, the first unit specific marker having a first label and the second unit specific marker including a second label distinct from the first label; exposing the labeled polymer to a detection station to produce distinct detection signals from the first and second labels; and identifying the distinct first and second signals (instant claim 1; see page 1, para 0008 of Chan-1). Chan-1 also teaches that the first unit specific marker can be different than the second unit specific marker, either in its nature or in the polymer unit it recognizes and binds to (instant claim 1; see page 1, para 0009 of Chan-1). Chan-1 also teaches that the first unit specific marker can be identical to the second unit specific marker, yet the first and second unit specific markers are labeled with distinct labels (instant claim 1; see page 1, para 0009 of Chan-1). Chan-1 also teaches that the polymer is preferably a nucleic acid that is genomic DNA (instant claim 1; see page 2, para 0013 of Chan-1) and that the unit specific marker can be a nucleic acid probe (instant claims 5 and 6; see page 8, para 0076 of Chan-1), or a peptide or polypeptide or peptide-nucleic acids (instant claims 5 and 6; see page 8, para 0077 of Chan-1). Chan-1 teaches that unit specific markers are attached to optically distinguishable labels that include a fluorescent molecule, a radioisotope, an enzyme, a biotin molecule, an avidin molecule, a semiconductor nanocrystal, a semiconductor nanoparticle, a colloid gold nanocrystal, a

micro bead, a protein, a peptide, a nucleic acid, a carbohydrate, an antigen, an antibody, etc. (instant claims 2-4; see page 3, para 0015 of Chan-1). Chan-1 teaches that the pattern of binding of the unit specific markers to the polymer may be determined using a variety of systems including a linear polymer analysis system (instant claim 1; see page 3, para 0033 of Chan-1) such as optical mapping or DNA combing. Chan-1 teaches that the unit specific marker (and thus the polymer) can be sequentially exposed to a station, "station" defined as a region where a portion of the polymer is exposed to an energy source in order to produce a signal or polymer dependent impulse, by movement of the marker and the station relative to one another (instant claim 1; see page 12, para 0109 of Chan-1). Chan-1 teaches that the polymer can be aligned and stretched before it reaches the interaction station and that a very effective technique of stretching DNA is to pass the polymer through a tapered microchannel having an obstacle field, followed by a constant-shear section to maintain the stretching obtained and straighten out any remaining coiling in the polymer (embodiment of "passing said hybridized DNA complex....." in instant claim 1.c; see page 13, para 0125 and page 14, para 0128 of Chan-1). Chan-1 also teaches that pressure flow is the preferred driving force of the DNA through such a microchannel recited above (see page 14, para 0128 of Chan-1). With regard to instant claim 1.d reciting "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex,...", the recitation is interpreted as detecting *one or more* optically distinguishable DNA sequence recognition units in a sequential manner along

a substantially linear hybridized DNA complex, which is taught by Chan-1 (see page 1, para 0008 and page 3, para 0033 of Chan-1).

8. Claims 1-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Hannah et al (hereinafter referred to as Hannah; U.S. Patent 6,767,731 B2, 102(e) date 08/27/2001).

Hannah teaches a method of sequencing a target nucleic acid comprising hybridization of the target DNA with probes, which can be oligonucleotides and oligonucleotide analogs that are uniquely and detectably labeled, using a microfluidic device to pass the hybridized nucleic acid through a microchannel to extend it to an approximate linear conformation by hydrodynamic focusing, and detecting the spectral signature of each labeled probe, preferably in sequential order (instant claims 1, 5 and 6; see column 2, lines 38-44 and 51-56, and column 3, lines 3-7 and 9-11 of Hannah). Hannah also teaches that nucleic acid molecules sequenced by this method can be DNA or RNA (instant claim 1; see column 4, lines 62-65 of Hannah). Hannah also teaches that the probes used for this method can be DNA, RNA, or analog thereof, such as a peptide nucleic acid (instant claims 5 and 6; see column 6, lines 30-34 of Hannah). Hannah also teaches that the probe labels can be fluorescent, luminescent, radioactive, phosphorescent, chemiluminescent, enzymatic, spin, electron dense, mass spectroscopic, semiconductor nanostructures, and quantum dots (instant claims 2-4; see column 8, lines 42-47 and column 10, lines 12-37 of Hannah). Hannah also teaches that photolithography can be used to obtain microchannels for use in linearizing

DNA in the range of tens of micrometers wide and deep (instant claims 7-9; see column 12, lines 14-16 of Hannah). With regard to instant claim 1.d reciting "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex,...", the recitation is interpreted as detecting *one or more* optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex, which is taught by Hannah (see column 2, lines 38-44 and 51-56, and column 3, lines 3-7 and 9-11 of Hannah).

Response to Arguments

9. The response traverses the rejections of Chan-1 and Hannah via filing of a declaration under 37 C.F.R. §1.131. The declaration asserts that the claimed invention was conceived by applicants Yang and Qiao prior to the US filing date of Hannah or Chan-1 as evidenced by the attached notebook page 154 dated 06/05/2001. The declaration further asserts that diligence was exercised in pursuing a patent application from the time of conception to the time of filing. This declaration has been thoroughly reviewed but was not found persuasive to overcome the rejections of Chan-1 and Hannah. The declaration does not state where the acts relied upon to establish the date of invention occurred. These acts must have occurred in the US, a NAFTA country, or a WTO member country as a requirement to show prior invention (see MPEP 715.07(c)). Currently Zhihao Yang, Tiecheng Qiao, Susan Muller, and Dorian Liepmann are listed as applicants for the instant application. It is noted that only Zhihao Yang has signed the declaration. It is disclosed in the declaration that Zhihao Yang and

Tiecheng Qiao conceived of the invention prior to the filing date of Hannah and Chan-1. It is acceptable for less than all of the inventors to sign to declaration where there is indication that not all of the named inventors invented the subject matter, however, all of the *contributing* inventors need to sign the declaration. However, the declaration under 37 C.F.R. §1.131 filed by the applicant is traversing the rejections by Chan-1 and Hannah with regard to all pending claims 1-8 and does not address who invented the *entire* claimed invention. Therefore, because the declaration does not state who invented the *entire* claimed invention and it is not clear as to whether all of the contributing applicants have signed the declaration, the declaration is deficient under 37 C.F.R. 1.131 (see MPEP 715.04). The declaration provides "notebook page 154" which discloses the steps of: a) attaching different oligonucleotides with different colored beads, b) hybridizing the labeled oligonucleotides with unknown DNA molecule, c) stretching the DNA molecules from random coil to linear confirmation under microscopy by a microfluidic device as shown in Berkeley, d) and recording the order of colored-beads to determine the species of DNA. The "Summary of Invention" on the last page of the declaration discloses that: a) a large DNA molecule can be stretched from a coil to linear conformation through a micro-channel by a micro-fluidic device, b) color beads or markers having specific oligonucleotides are present that hybridize at different sites of a single strand DNA molecule, c) therefore, when the molecule passes through the microchannel in a linear conformation, the order of color beads or makers can be read optically, and the sequence information of the DNA can be obtained. It is noted that several limitations of the instant claims are not disclosed by "notebook page 154" and

the "Summary of Invention". With regard to claim 1, part c), the "notebook page 154" and the "Summary of Invention" do not disclose any teachings of a "reservoir" from which the DNA is passed from. In addition claim 1, part c) recites passing the DNA "from a reservoir in a microfluidic device through a narrow channel to cause an acceleration of fluid flow through said channel, thereby causing said hybridized DNA complex to extend into a substantially linear confirmation". Although the "Summary of Invention" teaches that the DNA can be stretched from random coil to linear through a microchannel by a microfluidic device, it does not teach how the stretching of the DNA relates to the "acceleration of fluid flow through said channel" recited in instant claim 1. It is noted that because no further elaboration of "as shown in Berkeley" recited in "notebook page 154", part c) is given, this phrase is given no consideration with regard to the applicant's response because it is unclear how such recitation relates to the invention. Additionally, the "notebook page 154" and the "Summary of Invention" do not address further limitations of the claims such as "microparticles having different shapes" (claim 3), nanocrystals (claim 4), peptide nucleic acids (claim 5), protein scaffolds or "synthetic molecular moiety" (claim 6), or the width and depths of the narrow channels (claims 7 and 8). For these reasons and the reasons already made of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

10. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bensimon, in view of Chan-2 (hereinafter referred to as Chan-2; PCT/US00/22253, International Publication Number WO 01/13088 A1, International Publication Date 02/22/2001).

For the instant rejection, the recited phrase "from a reservoir in a microfluidic device " is interpreted as the hybridized DNA initially being in a separate chamber in a device having channels with dimensions in the micrometer range. In addition, passing the hybridized DNA complex through a "narrow channel to cause an acceleration of flow through said channel, thereby causing said hybridized DNA complex to extend into a substantially linear configuration;" is interpreted as the entire hybridized DNA complex being passed through a narrow channel and extended to a linear configuration due to the hydrodynamic forces associated with the accelerated microfluidic flow of the fluid containing the hybridized DNA complex through the channel.

Bensimon teaches a method of analyzing DNA comprising hybridizing the DNA in solution with probes having fluorescent reagents and then detecting the position of the probes after aligning ("causing said hybridized DNA complex to extend into a substantially linear configuration", instant claim 1.c) the DNA (instant claims 1, 5 and 6; see column 16, lines 50-55, and Fig. 6 of Bensimon). Bensimon also teaches that DNA molecules placed in a channel between cover slips can be aligned by the evaporation flow parallel to a moving meniscus in the channel (instant claim 1.c; see column 2, lines 11-12 and column 3, line 22 and Fig. 6 of Bensimon). Bensimon also teaches that the probes used to hybridize to DNA can be oligonucleotides, RNA, DNA, and peptide

nucleic acids (instant claims 5 and 6; see column 13, lines 21-23 and 64-65 of Bensimon). Bensimon also teaches that oligonucleotide probes can be labeled with fluorescent labels and microbeads (instant claims 2-4; see column 11, lines 20-41, and column 14, lines 4-7 of Bensimon). With regard to instant claim 1.d reciting "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex,...", the recitation is interpreted as detecting *one or more* optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex, which is taught by Bensimon (see column 16, lines 50-55 of Bensimon).

Bensimon does not teach a method of linearizing a hybridized DNA complex by hydrodynamic force employing a microfluidic device, having dimensions in the micrometer range, to pass the entire hybridized DNA complex from a separate reservoir into a narrow channel. However, Chan-2 teaches that since microfluidic devices allow multiple molecules to be stretched in succession, extremely high throughput screening can be achieved (instant claims 1-8; see page 20, lines 25-27 of Chan-2). In addition, Chan-2 teaches that the method of linearizing DNA used by Bensimon, known as "molecular combing", cannot be easily adapted to a high-throughput operation because the immobilization of the polymers is a rate-limiting step and further modification of the polymers is more difficult after immobilization (see page 5, lines 15-17 of Chan-2). Chan-2 also teaches that molecular combing and other polymer stretching techniques are lacking in the uniformity and reproducibility of stretching, ease of handling of the biopolymer, applicability to all types and sizes of biopolymers, and the ability to rapidly

analyze information (see page 7, lines 33-36 of Chan-2). Chan-2 also teaches detailed microfluidic polymer stretching structures, which enable stretching by hydrodynamic force, with various widths and depths and accompanying stretching methods (see Figures 1-23; page 26, lines 5-35; page 39, lines 29-36, and page 40, lines 1-10 of Chan-2). Specifically, Chan-2 teaches that a channel with 1 μm depth, 1 mm length, and a shear rate of 0.25/s gives a force of approximately 0.25 pN, which the inventors have verified experimentally is adequate to stretch DNA (instant claims 7 and 8; see page 25, lines 16-20 of Chan-2). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of linearizing DNA taught by Bensimon in the method of DNA analysis taught by Bensimon with the DNA linearzing method taught by Chan-2 because Chan-2 teaches that this method for linearizing DNA is capable of extremely high-throughput operation and allows rapid analysis on a reasonable timescale. The ordinary artisan would have been motivated to replace the method of linearizing DNA taught by Bensimon with the method of linearizing DNA taught by Chan-2 for the purpose of improving the method of Bensimon because Chan-2 teaches that molecular combing as taught Bensimon cannot be easily adapted to a high-throughput operation and is incapable of rapid analysis of information, while the method of Chan-2 is readily capable of extremely high-throughput operation and rapid analysis of information. In addition, Chan-2 teaches specific examples of microfluidic structures for stretching DNA with their dimensions and the methods for fabrication of such structures.

Response to Arguments

11. The response traverses this rejection. The response asserts that because Bensimon requires attachment of one end of the macromolecule to a surface, Bensimon with Chan-2 does not disclose or suggest passing a hybridized DNA complex from a reservoir through a narrow channel. This argument has been thoroughly reviewed but was not found persuasive. Claim 1 does not recite limitations regarding how much of the DNA complex is passed through the channel and the claims have been broadly interpreted to include the "reservoir" and "narrow channel" as being the same area, see above paragraph 6, therefore the method of Bensimon is interpreted as passing a DNA complex from a reservoir in a microfluidic device through a channel and therefore Bensimon is maintained as the primary reference in this rejection. For these reasons and the reasons already made of record, the rejection is maintained.

12. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan-1, in view of Chan et al (hereinafter referred to as Chan-2; PCT/US00/22253, International Publication Number WO 01/13088 A1, International Publication Date 02/22/2001).

Chan-1 teaches a method of analyzing a polymer comprising labeling the polymer with first and second unit specific makers, the first unit specific marker having a first label and the second unit specific marker including a second label distinct from the first label; exposing the labeled polymer to a detection station to produce distinct detection signals from the first and second labels; and identifying the distinct first and

second signals (instant claim 1; see page 1, para 0008 of Chan-1). Chan-1 also teaches that the first unit specific marker can be different than the second unit specific marker, either in its nature or in the polymer unit it recognizes and binds to (instant claim 1; see page 1, para 0009 of Chan-1). Chan-1 also teaches that the first unit specific marker can be identical to the second unit specific marker, yet the first and second unit specific markers are labeled with distinct labels (instant claim 1; see page 1, para 0009 of Chan-1). Chan-1 also teaches that the polymer is preferably a nucleic acid that is genomic DNA (instant claim 1; see page 2, para 0013 of Chan-1) and that the unit specific marker can be a nucleic acid probe (instant claims 5 and 6; see page 8, para 0076 of Chan-1), or a peptide or polypeptide or peptide-nucleic acids (instant claims 5 and 6; see page 8, para 0077 of Chan-1). Chan-1 teaches that unit specific markers are attached to optically distinguishable labels that include a fluorescent molecule, a radioisotope, an enzyme, a biotin molecule, an avidin molecule, a semiconductor nanocrystal, a semiconductor nanoparticle, a colloid gold nanocrystal, a micro bead, a protein, a peptide, a nucleic acid, a carbohydrate, an antigen, an antibody, etc. (instant claims 2-4; see page 3, para 0015 of Chan-1). Chan-1 teaches that the pattern of binding of the unit specific markers to the polymer may be determined using a variety of systems including a linear polymer analysis system (instant claim 1; see page 3, para 0033 of Chan-1) such as optical mapping or DNA combing. Chan-1 teaches that the unit specific marker (and thus the polymer) can be sequentially exposed to a station, "station" defined as a region where a portion of the polymer is exposed to an energy source in order to produce a signal or polymer dependent

impulse, by movement of the marker and the station relative to one another (instant claim 1; see page 12, para 0109 of Chan-1). Chan-1 teaches that the polymer can be aligned and stretched before it reaches the interaction station and that a very effective technique of stretching DNA is to pass the polymer through a tapered microchannel having an obstacle field, followed by a constant-shear section to maintain the stretching obtained and straighten out any remaining coiling in the polymer (embodiment of "passing said hybridized DNA complex....." in instant claim 1.c); see page 13, para 0125 and page 14, para 0128 of Chan-1). Chan-1 teaches that pressure flow is the preferred driving force of the DNA through such a microchannel recited above (see page 14, para 0128 of Chan-1). With regard to instant claim 1.d) reciting "detecting said optically distinguishable material in a sequential manner along said substantially linear hybridized DNA complex,...", the recitation is interpreted as detecting *one or more* optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex, which is taught by Chan-1 (see page 1, para 0008 and page 3, para 0033 of Chan-1).

Chan-1 teaches stretching DNA by passing the DNA through a microchannel, but is silent with respect to the width or depth of the channel (see page 13, para 0125 and page 14, para 0128 of Chan-1). However, Chan-2 teaches that a channel with 1 μm depth, 1 mm length, and a shear rate of 0.25/s gives a force of approximately 0.25 pN, which the inventors have verified experimentally is adequate to stretch DNA (instant claims 7 and 8; see page 25, line 16 of Chan-2). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to

perform the method of Chan-1 with the device of Chan-2 because Chan-2 specifically teaches a device for performing the method of Chan-1. The ordinary artisan would have been motivated to use the device of Chan-2 because Chan-1, while generally teaching a method of stretching DNA with a microfluidic device, is silent with regard to the specific structure and dimensions of the device. The device, with its specific dimensions, taught by Chan-2 functions to stretch DNA as taught by Chan-1. The ordinary artisan would be motivated to use the device of Chan-2 in the method of Chan-1 because Chan-1 teaches to stretch DNA by passing the DNA through a microchannel, but no specific structure or dimensions of the microchannel are recited.

Response to Arguments

13. The response traverses this rejection via filing of a declaration under 37 C.F.R. §1.131. For the reasons discussed in paragraph 9 above, this declaration does not over come the rejection by Chan-1 with regard to claims 1-6. With regard to the further limitations of claims 7 and 8, it is noted that neither the "notebook page 154" or the "Summary of Invention" in the declaration teaches any dimensions of the "narrow channel" of the microfluidic device. For these reasons and the reasons already made of record, the rejection is maintained.

Conclusion

14. No claims are allowed.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas O'Farrell whose telephone number is (571) 272-8782. The examiner can normally be reached Monday-Friday from 8:30 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Thomas O'Farrell
Examiner
Art Unit 1634

Thomas J O'Farrell
12/13/05

Jehanne Sitton
JEHANNE SITTON
PRIMARY EXAMINER
12/15/05